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16. ABSTRACT

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Frequency-Dependent Absorption of Electromagnetic Energy in Biological Tissue

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Abstract—**The frequency-dependent absorption of electromagnetic energy in biological tissue is illustrated by use of the Debye equations, model calculations for different irradiation conditions, and measured electrical properties (conductivity and permittivity) of different tissues. Four separate irradiation conditions are treated for calculating the power absorbed in a given tissue when it forms a flat interface or is surrounded by another tissue. The calculations show that the greatest differential absorption occurs at frequencies between the dominant relaxation frequencies in the two tissues. From rat mammary gland tumor data, the calculations show an optimum frequency range of about 100–500 MHz for microwave hyperthermia treatment of at least these types of tumor.**

I. Introduction and Theory

FOR an electromagnetic wave propagating within a biological system, two adjacent tissues (e.g., muscle/fat, malignant/normal) will absorb power per unit volume (P_a in W/m^3) in the ratio

$$\frac{P_{a2}}{P_{a1}} = \frac{\sigma_2}{\sigma_1}\left|\frac{E_2}{E_1}\right|^2 \tag{1}$$

where σ is the tissue's electrical conductivity (mhos/m), E is the electric field intensity (V/m) within the tissue, and the subscripts denote each tissue. At frequencies within the 100-500 MHz range and below, the irradiated tissue will be within the near field of typical applicators. The plane-wave approximation is used herein, even though part of the power that flows within the near field of an applicator is not a uniform plane wave. For noninvasive applicators, this approximation is expected to have a negligible effect upon the results obtained.

We explore the frequency-dependent absorption in (1) that renders $P_{a2} > P_{a1}$ under four representative irradiation conditions.

1) An electromagnetic (EM) wave propagating within each tissue with the electric field vector parallel to the interface between the tissues. Thus, the direction of propagation can be either parallel or perpendicular to the common interface.

2) An EM wave propagating along the interface in both tissues with the electric field vector perpendicular to the interface between tissues.

3) An EM wave incident upon tissue 2 from 1, where tissue 2 is a sphere of radius a surrounded by tissue 1, and the radius a is small compared to wavelength (λ_1) in tissue 1.

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4) Same as condition 3) except that tissue 2 is a long cylinder of radius a, and the electric field vector and the propagation direction are both perpendicular to the axis of the cylinder.

In condition 1), the electric field intensities are tangent to the interface between tissues 1 and 2. Therefore $E_1 = E_2$ as a boundary condition, and (1) becomes

$$\frac{P_{a2}}{P_{a1}} = \frac{\sigma_2}{\sigma_1}. \tag{2}$$

Hence, at frequencies (f) where $\sigma_2 > \sigma_1$, tissue 2 absorbs a greater volume power density than tissue 1.

In condition 2), the electric fields are perpendicular to the common interface and they cause conduction and displacement currents that must be continuous across the interface, as [1]

$$(\sigma_2 + j\omega\epsilon_2)E_2 = (\sigma_1 + j\omega\epsilon_1)E_1 \tag{3}$$

or

$$\left|\frac{E_2}{E_1}\right|^2 = \frac{\sigma_1^2 + \omega^2\epsilon_1^2}{\sigma_2^2 + \omega^2\epsilon_2^2} \tag{4}$$

where ϵ is the electrical permittivity of the respective tissue and ω is the radian frequency. Thus, we have from (4) and (1)

$$\frac{P_{a2}}{P_{a1}} = \frac{\sigma_2}{\sigma_1}\left(\frac{\epsilon_1}{\epsilon_2}\right)^2 \frac{1 + (\sigma_1/\omega\epsilon_1)^2}{1 + (\sigma_2/\omega\epsilon_2)^2}. \tag{5}$$

Since the terms in (5) appear again later, we delay any evaluation of (5) until P_{a2}/P_{a1} for the final two conditions are expressed.

For condition 3), since the sphere is small compared to wavelength, the ratio of electric field intensity inside the sphere (tissue 2) to the incident field intensity in tissue 1 is [2]

$$\frac{E_2}{E_1} = \frac{3}{2 + \dfrac{\epsilon_2^*}{\epsilon_1^*}} \tag{6}$$

where

$$\frac{\epsilon_2^*}{\epsilon_1^*} = \frac{\epsilon_2 - j\sigma_2/\omega}{\epsilon_1 - j\sigma_1/\omega} = \frac{\epsilon_2\left(1 - j\dfrac{\sigma_2}{\omega\epsilon_2}\right)}{\epsilon_1\left(1 - j\dfrac{\sigma_1}{\omega\epsilon_1}\right)}. \tag{7}$$

Thus, from (6) and (7)

$$\frac{E_2}{E_1}=\frac{3(1-j\sigma_1/\omega\epsilon_1)}{2+\frac{\epsilon_2}{\epsilon_1}-j\left(\frac{2\sigma_1}{\omega\epsilon_1}+\frac{\sigma_2}{\omega\epsilon_1}\right)} \tag{8}$$

and substitution into (1) yields

$$\frac{P_{a2}}{P_{a1}}=\frac{\sigma_2}{\sigma_1}\,\frac{9[1+(\sigma_1/\omega\epsilon_1)^2]}{\left(2+\frac{\epsilon_2}{\epsilon_1}\right)^2+\left(\frac{2\sigma_1}{\omega\epsilon_1}+\frac{\sigma_2}{\omega\epsilon_1}\right)^2}. \tag{9}$$

For condition 4), the cylinder radius is small compared to a wavelength, and the ratio of electric field intensity in tissue 2 (cylinder) to the incident field in tissue 1 is [2]

$$\frac{E_2}{E_1}=\frac{2}{1+\frac{\epsilon_2^*}{\epsilon_1^*}}. \tag{10}$$

Using (7) in (10), we have

$$\frac{E_2}{E_1}=\frac{2(1-j\sigma_1/\omega\epsilon_1)}{\left(1+\frac{\epsilon_2}{\epsilon_1}\right)-j\left(\frac{\sigma_1}{\omega\epsilon_1}+\frac{\sigma_2}{\omega\epsilon_1}\right)}. \tag{11}$$

Thus, from (11) and (1)

$$\frac{P_{a2}}{P_{a1}}=\frac{\sigma_2}{\sigma_1}\,\frac{4[1+(\sigma_1/\omega\epsilon_1)^2]}{\left(1+\frac{\epsilon_2}{\epsilon_1}\right)^2+\left(\frac{\sigma_1}{\omega\epsilon_1}+\frac{\sigma_2}{\omega\epsilon_1}\right)^2}. \tag{12}$$

To determine P_{a2}/P_{a1} for the four irradiation conditions at a given frequency, we must also examine the frequency dependence of σ and ϵ. The frequency dependence of σ and ϵ is directly related to the polarization of molecules and structural interfaces as a result of the applied electric field within the biological tissue. A specific polarization effect is important in determining σ and ϵ up to a relaxation frequency (f_r) where the induced polarization can no longer change as fast as the applied field [3]-[5]. Structural or Maxwell-Wagner relaxation because of cellular membranes and other layered structures within the tissue is of importance at frequencies below about 30-100 MHz [5], [13]. Polar or Debye relaxation because of the rotation of molecules or molecular groups by the applied field is of prime importance in determining σ and ϵ at microwave frequencies. In the 30-2000 MHz range, the frequency dependence of σ and ϵ for tissue is dominated mostly by free water (f_r = 25 000 MHz); however, bound water (f_r of 100-1000 MHz) and protein molecules (f_r of 40-300 MHz) make significant contributions as well [5]-[7].

Because most types of polarization can be described formally in the same qualitative manner, the Debye equations often apply very well, even though they were derived for the case of molecular rotation. For a given relaxation frequency, the Debye relations for σ and ϵ are expressed as [3], [8]

$$\sigma=\sigma_L+\frac{(\epsilon_L-\epsilon_H)2\pi f_r}{1+\left(\frac{f_r}{f}\right)^2} \tag{13}$$

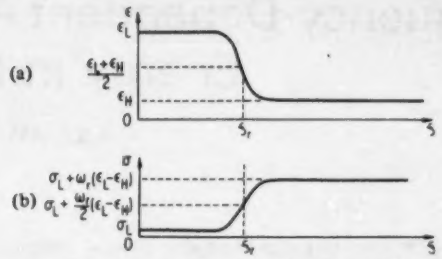

Fig. 1. Plot of Debye equations giving (a) permittivity and (b) conductivity frequency.

and

$$\epsilon=\epsilon_H+\frac{\epsilon_L-\epsilon_H}{1+\left(\frac{f}{f_r}\right)^2} \tag{14}$$

where $\epsilon=\epsilon_H$ at $f\gg f_r$, and $\sigma=\sigma_L$, $\epsilon=\epsilon_L$ at $f\ll f_r$. The frequency variation of the Debye equations is sketched in Fig. 1. Note that when $f=f_r$, $\sigma/\omega\epsilon$ is near unity in value if, as usually assumed, $\epsilon_L\gg\epsilon_H$ and $\sigma_L\ll\omega_r\epsilon_L$.

Using the Debye equations for two tissues having widely separated relaxation frequencies f_{r1} and f_{r2}, the theoretical variations of σ and ϵ versus frequency are shown in Fig. 2. Of particular interest in Fig. 2 is some operating frequency f, that lies between f_{r2} and f_{r1}, where both σ_2/σ_1 and ϵ_1/ϵ_2 are larger than they would be at frequencies outside this range. Referring back to (2), (5), (9), and (12), we observe that σ_2/σ_1 and ϵ_1/ϵ_2 are also the ratios that should be maximized in order to maximize P_{a2}/P_{a1}. Hence, from this simple model of two adjacent tissues, we would expect P_{a2}/P_{a1} to be larger at an applied frequency (f) that lies between f_{r2} and f_{r1} than at frequencies below f_{r2} or above f_{r1}.

While this illustration may serve as a guide in locating frequencies that produce the greatest P_{a2}/P_{a1}, the dominant relaxation frequencies in adjacent tissues may not be widely separated or well defined. In fact, the tissue may exhibit several relaxation frequencies due to constituent materials. In all instances, however, the more general expressions for P_{a2}/P_{a1} in (2), (5), (9), and (12) yield valid results if σ and ϵ are known at each frequency of interest. Examples of this more practical situation will now be given.

II. Calculations from Measured Data

An important application of the power absorption equations is in the case of malignant tissue adjacent to, or surrounded by, normal tissue. There are reasons to expect a difference in electrical properties between normal and malignant tissue. Cancer cells are reported to have an excess of sodium, which not only affects the membrane potential of cells [9]-[11], but causes malignant tissue to retain more fluid than normal tissue [12], [13]. The excess sodium and fluid alone would yield greater conductivity (σ) and permittivity (ϵ) values in malignant tissue than in normal tissue. But, in addition, the fluid is believed to be retained in the form of bound water, which has larger values of σ and ϵ than free water since the relaxation frequency (f_r) of bound water is

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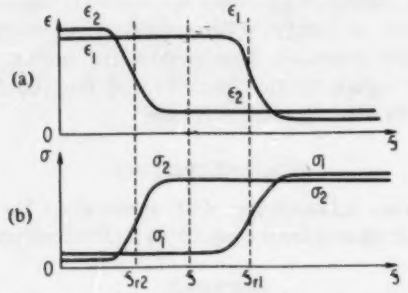

Fig. 2. Plot of Debye equations giving (a) permittivity and (b) conductivity of two materials (designated by subscripts 1 and 2) with widely separated relaxation frequencies.

within the 100-1000 MHz range, whereas f_r for free water is about 25 000 MHz at 37°C [7], [14].

Measurements made by a number of researchers have shown that malignant tissues have a significantly higher water content than does normal tissue [13]-[16]. For example, skin carcinoma has 34 percent more water content than normal skin [16], and liver hepatoma tissue has about 15 percent more water than normal liver tissue [15]. In addition, nuclear magnetic resonance measurements indicate that the water content of tumorous rat tissue is 36 percent greater than in the corresponding normal tissue [17].

The frequency-dependent values of σ and ϵ for SMT-2A mammary gland tumors and for normal adjacent muscle and mammary tissues have been determined by measurements and by curve-fitting using the Debye equations [8]. These measurements were made *in vivo* over the 30-2000 MHz range using an open-ended coaxial probe. The resulting values of σ and ϵ are graphed in Fig. 3.

The measured values of σ and ϵ in Fig. 3 are for the composite *in vivo* structure of skin over malignant tissue, muscle tissue, or mammary tissue. Hence, these values of σ and ϵ should not be compared directly to values of σ and ϵ measured on excised homogeneous tissue. Also, since the mammary gland in female W/Fu isogeneic rats occupies a somewhat smaller volume than the fringing field region of the open-ended probe, the mammary gland data will be influenced to some extent by adjacent muscle tissue. These are inherent limitations of the *in vivo* measurements. By performing the ratio P_{a2} for malignant tissue (plus the skin layer) to P_{a1} for muscle tissue (plus skin) or mammary tissue (plus skin), the effect of the common layer of skin tends to cancel out.

III. Results and Discussion

The results of using the SMT-2A/mammary gland data from Fig. 3 to calculate P_{a2}/P_{a1} are displayed in Fig. 4 for the irradiation conditions represented by (2), (5), (9), and (12). The results of using SMT-2A as tissue 2 and muscle as tissue 1 are similar but the peaks are smaller, as illustrated in Fig. 5. Since the SMT-2A data are from mammary gland tumors, the results in Fig. 4 may more appropriately represent a true-to-life situation. One observes from Fig. 4 that the greatest absorption ratio occurs for condition 1) (E parallel to interface) at about 225 MHz, followed by peak absorptions for condition 3) (sphere of SMT-2A) at about 350 MHz, condition 4) (cylinder of SMT-2A) at about 400 MHz, and condition 2) (E perpendicular to interface) at about 450 MHz. Since

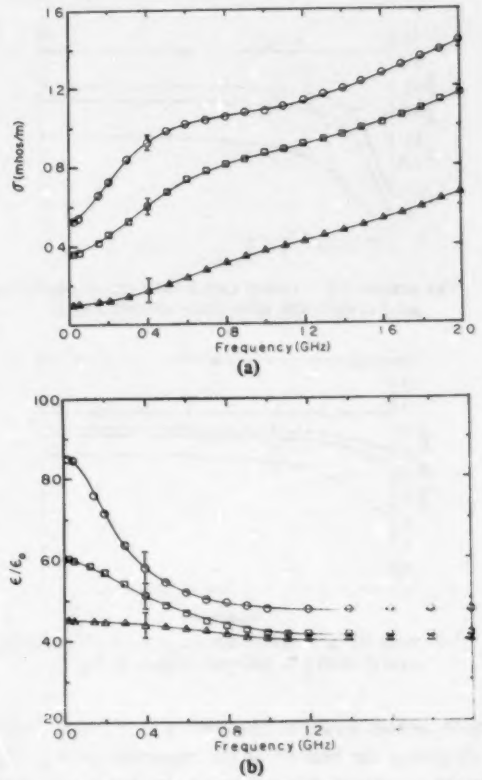

Fig. 3. (a) Conductivity (σ) of SMT-2A (circles), muscle (squares), and mammary (triangles) tissue versus frequency from 30 to 2000 MHz. (b) Relative permittivity (ϵ/ϵ_0) of the same three tissues.

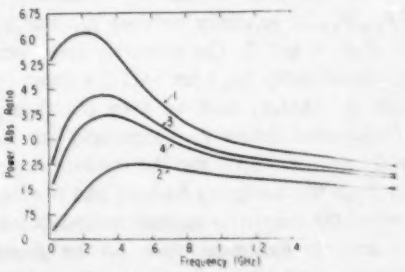

Fig. 4. Plot of power absorption ratio P_{a2}/P_{a1} versus frequency with SMT-2A and mammary from Fig. 3 as tissues 2 and 1, respectively, for the irradiation conditions: 1) E parallel to interface, 2) E perpendicular to interface, 3) tissue 2 sphere within tissue 1, and 4) tissue 2 cylinder within tissue 1.

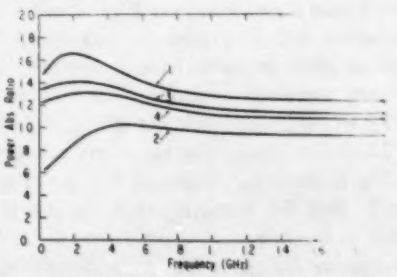

Fig. 5. The same as Fig. 4 except that muscle (from Fig. 3) is tissue 1.

tumors embedded in normal tissue are irregularly shaped in general, all of these conditions may apply during hyperthermia treatment of tumors using microwave irradiation. Hence, from these data the optimum frequency range for microwave

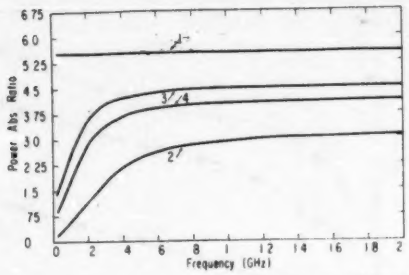

Fig. 6. The same as Fig. 4 except that σ and ϵ are arbitrarily held constant at their 400 MHz values given in Fig. 3.

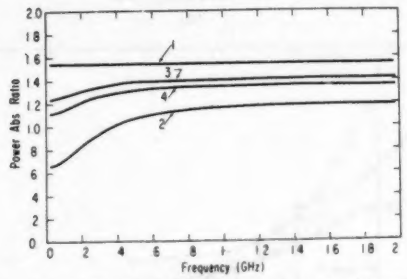

Fig. 7. The same as Fig. 5 except that σ and ϵ are arbitrarily held constant at their 400 MHz values given in Fig. 3.

heating of tumors would extend from about 100 to 500 MHz.

In obtaining the best fit of the measured data in Fig. 3 to the Debye equations, the relaxation frequencies for SMT-2A, muscle, and mammary tissue were selected to be 275, 500, and 1100 MHz, respectively [8]. Hence, for this example application of the four irradiation conditions, the largest values of P_{a2}/P_{a1} lie generally between f_{r1} and f_{r2}, as can be seen from Figs. 4 and 5. The relatively large values of low-frequency conductivity (σ_L) for SMT-2A tissue (perhaps due to the sodium content) tend to keep the absorption ratios high at frequencies below f_{r2}, especially for condition 1) where the absorption ratio is also the conductivity ratio.

As seen from the foregoing analysis and results, two major factors control the frequency-dependent absorption of electromagnetic energy in biological tissue: a) the geometry of the absorbing tissue, and b) the frequency dependence of σ and ϵ for adjacent tissues. Factor a) is quite evident from Figs. 4 and 5 because it is only the difference in geometry that offsets one relative absorption curve from another. The contribution of factor b) can be illustrated by retaining the four different geometrical conditions as in Figs. 4 and 5, but holding σ and ϵ constant with frequency for each tissue. Fixing σ and ϵ at the values given for each tissue at 400 MHz in Fig. 3, the SMT-2A/mammary gland absorption ratios as calculated from (2), (5), (9), and (12) are displayed in Fig. 6. In like manner, the SMT-2A/muscle absorption ratios are calculated and displayed in Fig. 7. Note by comparing Fig. 6 to Fig. 4, and Fig. 7 to Fig. 5, that the high-frequency decline in absorption ratios is due to the frequency dependence of σ and ϵ, and that the low-frequency decline in absorption ratios is mainly due to the geometry factor [except for condition 1), where the absorption ratio is the ratio of conductivities].

While maximizing the ratio of absorbed power is an important consideration, other parameters are also important in choosing an optimum frequency for hyperthermia applications. The primary requirement is the need to deliver a sufficient amount of energy, with reasonable uniformity, to the region of the tumor. For deeply-embedded tumors, the more penetrative signals at the lower end of the 100-500 MHz range may be most appropriate for use.

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